

## REMARKS

Claims 1-6 have been canceled. Claims 7-18 are currently under examination.

In the January 25th communication, the Examiner indicated that all rejections have been withdrawn except the rejections under 35 U.S.C. §112 and the obvious-type double-patenting rejection in view of U.S. Patent 6,872,399. In view of the following, reconsideration of such rejections is respectfully requested.

### Section 112 Rejection

Claims 7-18 have been rejected under 35 U.S.C. §112, first paragraph for allegedly failing to comply with the enablement requirement. According to the Office Action, the specification does not set forth enablement of a vaccine comprising 4 or more inactivated dermatophyte strains.

Applicants respectfully disagree. “When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement”. *In re Wright*, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993) (emphasis added). See also *In re Morehouse*, U.S.P.Q. 29, 32 (CCPA 1976).

Upon careful review of the previous Office Action dated January 25, 2006, no proper explanation or sufficient reasons were given by the Examiner as to why the scope of protection provided by the claims is allegedly not enabled by the specification. In fact the Examiner has already agreed that the specification is enabling for the use of the inactivated strain in a vaccine composition:

“Claim 18, 21-23, 34 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for use of the inactivated strain**, does not reasonably provide enablement for one antigen from the dermatophytes, *T. verrucosum*, to be used in the vaccine

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composition.” (Final Office Action dated August 29, 2001 for related application 09/256,915, to which benefit is claimed in the subject application, page 3 at 6) (emphasis added).

Similarly, the Examiner has stated:

Applicants have asserted that the immunogenic response produced by immunization of an animal with a vaccine comprising a single inactivated strain, as described in Table 1-7 establishes (results) in immunity to that strain. The Examiner agrees that administration of **a single inactivated strain establishes immunity**, however an immune response does not establish vaccine protection against dermatomycosis as presently claimed by Applicants. (Office Action at page 5, second paragraph) (emphasis added).

Applicants fully agree with Examiner’s conclusion that the specification is fully enabling for the use of any of the inactivated strains. Accordingly, if the use of a vaccine containing only one inactivated strain is considered to be disclosed in an enabling manner, how can the use of a vaccine containing four, five, six, seven or eight of such strains not be considered to be disclosed in an enabling manner? In short, if a vaccine comprising one strain is shown to provide immunity and to comply with the requirements of 35 U.S.C. 112, first paragraph, why should a vaccine comprising several of said strains not provide immunity? If the Examiner’s concerns are based on the recitation of vaccine, please see the comments beginning on page 14 below.

The Examiner put forward several, unsupported allegations as discussed below:

- (a) “It is not clear what Applicants used in the vaccine composition. Example 1, page 18 indicates that “[A]fter 2 days, 125 ml of each culture in suspension is taken and mixed in a single container. The vaccine may be prepared by mixing together various combinations of the given strains.” Exactly what was the composition of the vaccine administered that gave the results found in Tables 9 and 10? It is not clear if all 8 dermatophytes were used or some combinations of 3, 4, 6 or 7 dermatophytes. It is not clear that the specific combination of 3 dermatophytes as set forth in claim 2 were used.” (Office Action at page 3, first paragraph).
- (b) “Specifically, the specification has not taught how to use the claimed vaccine. Mixing each culture in a single container or mixing together various combinations of the given cultures is set forth. However, it is not clear which composition (all 8 cultures in one container or various combinations of less than 8 cultures and if less than 8 cultures specifically which ones) was used to generate the data found on tables 9 and 10 of the specification.” (Office Action at page 3, second paragraph).
- (c) “Does Applicant intend for “immunogenic response” to mean that vaccine protection has been established, see page 11, or “establishing immunity” to mean vaccine protection has been established, see Tables 1-7?” (Office Action at page 3, first paragraph). The Examiner further cites Gudding et al (Can. Vet. J. 1995) and continues “Further, the inactivated vaccine against ringworm must be capable of eliciting both humoral and cellular immune responses, of which the cellular immune response is crucial for protection and adjuvants are important in stimulating the cellular branch of the immune system (pp. 303-304). In view of the state of the art it is not clear if protection has been established against ringworm infection when Applicants state (see tables 1-7) “establishes immunity”. It is not clear what type of immunity is established. Applicant’s vaccine composition does not recite a carrier or adjuvant, however Gudding indicates that the adjuvants are important in stimulating the cellular branch of the immune system and the cellular branch is crucial for protection. (Office Action at page 4, second paragraph)

#### **Allegation (a)**

With regard to allegation (a), the Examiner has cited only part of Example 1. Omitted is the preceding paragraph:

“To produce 1 liter of vaccine, cultures are taken of the strains VKPGF-931/410, 930/1032, 929/381, 551/68, 928/1393, 727/1311, 728/120, and 729/59 and grown in agar/wort at 26°C for 15 days. Each culture is grown

in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer. The solution used is an aqueous solution containing 1% fermented hydrolyzed muscle protein, 10% glucose and 1% yeast extract. The concentration of microconidia is brought to 90 million per ml of homogenate. After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container.” (emphasis added)

Therefore, from the quoted wording, it is clear to the skilled person that in cited Example 1 the 8-fold vaccine, as covered by claim 7, was prepared and used in prophylaxis and therapy.

The sentence “The vaccine may be prepared by mixing together various combinations of the given strains” (emphasis added), uses the term “may” which clearly indicates to the skilled person what optionally may be done, e.g. instead of eight strains, the combination of four, five, six, and seven strains as recited in claims 7-18 may be used in a vaccine according to the invention.

#### **Allegation (b)**

Regarding allegation (b), the wording of Example 1 clearly states that each of the eight cultures is first cultured separately and homogenized:

“Each culture is grown in 8 mattress flasks. The fungal mass is then lifted off, homogenized, placed in 200 ml of solution and added to each mixer.”

and then combined into one container:

“After 2 days, 125 ml of each culture in suspension is taken and mixed in a single container.”

Further, the specification extensively describes immunizing the animals using the vaccine prepared in Example 1 to determine dosage to be given and the method of administration for prevention and treatment in ten different animal families (page 18, line 33 and Table 8). The effectiveness of the vaccine in preventing disease in 24 animal species is given (Example 2, page 21, and Table 9); and the effectiveness of the vaccine in treating infected animals in 18 different animal species is provided (Example 3, page 21 and Table 10).

Furthermore, clarification can also be drawn from page 3, lines 5-12 and 20-22 disclosing preferred vaccine combinations in the context of page 4, lines 8-18:

Page 3, lines 5-12:

This aim has been achieved by using the following fungal strains as vaccinal strains: *Trichophyton verrucosum* (especially No. VKPGF-931/410), *Trichophyton mentagrophytes* (especially No. VKPGF-930/1032), *Trichophyton equinum* (especially No. VKPGF-929/381), *Trichophyton sarkisovii* (especially No. VKPGF-551/68), *Microsporum canis* (especially No. VKPGF-928/1393), *Microsporum canis* var. *obesum* (especially No. VKPGF-727/1311), *Microsporum canis* var. *distortum* (especially No. VKPGF-728/120), *Microsporum gypseum* (especially No. VKPGF-729/59). Vaccines can be produced by using various combinations of antigenic material from the above strains together with a suitable carrier.

Page 3, lines 20-22:

“Another preferred combination of vaccine strains consists of *Trichophyton verrucosum* No. VKPGF-931/410, *Trichophyton mentagrophytes* No. VKPGF-930/1032, *Trichophyton sarkisovii* No. VKPGF-551/68, particularly for use in cattle.”

Page 4, lines 8-18:

In order to prepare a vaccine the following procedure may be used, for example:

Cultures of the strains are homogenized in an aqueous solution containing 0.2 to 2.0% fermented, hydrolyzed muscle protein (FGM-s), 5 to 12% glucose and 0.1 to 1.2% yeast extract. The concentration of the microconidia is adjusted to 40 to 120 million per milliliter and after 1 to 2 days the mixture is inactivated, *e.g.*, with thiomersal ( $C_9H_9O_2SNaHg$ ) in the ratio 1:10,000 to 1:25,000, or with another substance known from the prior art. The resulting suspension is packaged and is ready for use in animals.

The preparation of the vaccines, the dosage to be given and the method of administration for prevention and therapeutic treatment are explained in Examples 1 to 3.

With the before-mentioned extensive guidance provided to the skilled person, Applicants have shown how to make and use both vaccines within the scope of the claims.

Furthermore, the Examiner did not consider and apply the factors and analysis of *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988) and *Ex parte Forman*, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986). In properly considering and applying the factors concerning enablement, the following factors should be considered: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

With regard to factors (1) and (2), to practice the invention, either 4 or more dermatophytes must be grown, mixed together in a single container, the mixture is inactivated, and the resulting vaccine is bottled (described in the specification on

pages 4, lines 10-18, page 18, lines 15-31), and applied to animals at a dosage and with a route of administration as disclosed in Example 2, page 21, and Table 9 (prevention) as well as Example 3, page 21 and Table 10 (therapy). As set out *supra*, the dosage and route of administration is given for 10 different animal families, and guidance regarding efficacy of the 8-fold vaccine is given for 24 animal species (prevention) and 18 animal species (therapy) all of which represents a very limited amount of routine experimentation under a significant amount of guidance presented in the specification. If at all, there is minimal routine experimentation necessary to test a 4 or more fold vaccine in a similar manner as the 8-fold vaccine. With regard to factor (3), there are several in-depth working examples disclosing the preparation of vaccines according to the invention, the dosage, the route of preventive or therapeutic administration for numerous animal species. With regard to factors (4), (5), (6), and (7), as the nature of the invention is in the immunology, animal health and vaccine art, which is very highly developed, the state of the prior art is high, and the relative skill of those in the art is at a very high level, one would expect one of skill in the art would easily be able to use the directions in the specification to make and use the vaccines according to the invention. Regarding factor (8), it should be pointed out again that the claims presented for review recite specific vaccines consisting of four or more specified dermatophytes.

This situation is in contrast to that of *Ex parte Forman*, where the art was “undeveloped”, that at the time (early 1980s) “experiments in genetic engineering produce, at best, unpredictable results”, there were no apparent reproducible working examples presented outside the scope of the deposited microorganism strains, nor did there “appear to be ... a single detailed example that could be followed by another worker in another lab to obtain a single specific microorganism (vaccine) within Applicants’ claims, without recourse to the deposited strains recited in the allowed claims.” *Ex parte Forman*, at 548. The instant situation is more like *In re Wands*, where enablement was shown, as Applicants’ disclosure, like Wands’ disclosure, “provides considerable direction and guidance on how to practice their invention and

presents working examples. There was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known.” *In re Wands* at 1406.

35 U.S.C. § 112, first paragraph, certainly does not require each and every embodiment of the invention to be exemplified. Even the lack of a working example (quite contrary to the situation here with several working examples), if all the other factors point to enablement, is not considered to render the invention non-enabled, if one skilled in the art will be able to practice it without an undue amount of experimentation (M.P.E.P. 2164.02; *In re Borkowski*, 164 U.S.P.Q. 642, 645 (CCPA 1970)).

Further, the test is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue (M.P.E.P. § 2164.01; *In re Angstadt*, 190 U.S.P.Q. 214, 219 (CCPA 1976); *Atlas Powder Co. v. E.I. DuPont De Nemours & Co.*, U.S.P.Q. 409, 413 (Fed. Cir. 1984). The test [for undue experimentation] is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *The Johns Hopkins University v. Cellpro Inc.* 47 U.S.P.Q.2d 1705, 1719; *PPG Indus., Inc. v. Guardian Indus. Corp.* 37 U.S.P.Q.2d 1618, 1623 (emphasis added).

With the significant amount of guidance presented in the specification, the minimal routine experimentation necessary to test a 4-fold or more vaccine in a similar manner as the 8-fold vaccine can certainly not be considered undue.

#### **Allegation (c)**

With regard to allegation (c), Applicants cite Taber’s cyclopedic medical dictionary, in existence since 1940 and clearly the standard to the skilled person

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(Exhibit A). It is appropriate to compare the meaning of terms given in technical dictionaries in order to ascertain the accepted meaning of a term in the art. *In re Barr*, 170 U.S.P.Q. 330 (CCPA 1971).

“Vaccine” is defined to be used as follows:

“FUNCTION: Vaccines are used to stimulate **an immune response** in the body by creating antibodies or activated T lymphocytes capable of controlling the organism. **The result is protection against disease**; the duration depends on the particular vaccine (emphasis added).”

Therefore, for the use of a vaccine to be enabled, it is fully sufficient to stimulate an immune response which can either be the generation of antibodies or activated T lymphocytes, both requirements do not need to be satisfied. The Examiner’s arbitrary requirement of requiring both humoral (antibody-mediated) and cellular (T lymphocyte) responses is neither scientifically justified nor founded in the law. To fulfill the requirements of 35 U.S.C. § 112, first paragraph, it is fully sufficient that the vaccines according to the invention provide an immune response. This is extensively exemplified in Examples 2 and 3, page 21, and Tables 9 and 10 of the specification.

Likewise, the Examiner’s arbitrary requirement for an adjuvant to be present in the vaccine is neither scientifically justified nor founded in the law as discussed *infra*. Applicants successfully sell Insol® Dermatophyton and Insol® Trichophyton, presented for review (package inserts presented in Exhibits B and C, respectively). Both vaccines do not require adjuvants due to the superior properties of the vaccine strains contained therein. Thus, it is again respectfully submitted that the subject matter claimed fully complies with the requirements set forth in 35 U.S.C. § 112, first paragraph.

In many of these allegations, the Examiner seems to be attempting to shift the burden to the Applicants to affirmatively prove that Applicants are entitled to a patent, when it is the Examiner’s burden to prove that Applicants are not entitled to a patent

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with rejections that are supported by evidence and a rational basis. This the Examiner has not done.

Furthermore, Applicants respectfully direct the Examiner's attention to the Declaration of Dr. Igor Polyakov under 37 C.F.R. §1.132 ("the Declaration"). As stated in paragraph 5 of the Declaration, the vaccines of the present invention which are described in the Declaration were prepared essentially according to the method disclosed in the instant application. The minor, insubstantial differences between the method for preparing the vaccines disclosed in the above-identified application and the methods described in the Declaration are described in paragraph 6 of the Declaration. As is stated in paragraph 6 and demonstrated in paragraph 7 of the Declaration, such minor differences had no significant effect on the properties of the vaccines. Further, all of the challenge experiments were performed in the absence of adjuvants (paragraph 5).

Applicants further direct the Examiner's attention to paragraphs 8-12 of the Declaration wherein production and efficacy of dermatomycosis vaccines comprising four and five fungal strains is described. Results of these experiments are presented in Table 1, Examples 2-6. The experiments and results in paragraphs 8-12 correspond to new claims 8, 11, 9, 10, and 14, respectively. Production and efficacy of dermatomycosis vaccines comprising a single fungal strain is described in paragraph 13 of the Declaration; results of these experiments are presented in Table 1, Example 7.

With respect to the declaration, the Examiner states that "in order for a declaration to provide support for enablement of the claimed invention the results/data shown in the declaration have to have been performed by the exact same (i.e. identical) procedure as described in the filed specification." (Office Action page 6). Applicants are not aware of any authority requiring the exact same (i.e. identical) procedure. Rather, the guidance of the specification as well as what was well known to one of skill in the art is to be considered.

The experiments described in the Polyakov declaration are supported by whole disclosure of the specification, including any minor differences the experimental design of the Polyakov studies provided with declaration may have with the design of the experiments described in the section “Examples” of the patent application. For example, on page 4, lines 10 to 15 of the specification the conditions for the preparation of the vaccines are described in a general manner: “Cultures of the strains are homogenized in an aqueous solution containing 0.2 to 2.0% fermented, hydrolyzed muscle protein (FGM-s), 5 to 12% glucose and 0.1 to 1.2% yeast extract. The concentration of the microconidia is adjusted to 4 to 120 million per milliliter and after 1 to 2 days the mixture is inactivated, e.g., with thiomersal (C<sub>9</sub>H<sub>9</sub>O<sub>2</sub>SNaHg) in the ration 1:10,000 to 1:25,000, or with another substance known from the prior art. The resulting suspension is packaged and is ready for use in animals.”

Moreover, from page 2, line 15 of the specification it is known, that “Preparations, which are cultivated in agar/wort for 20-25 days at a temperature of 26-28°C.” On page 3, lines 28 to 30 of the specification it is mentioned that “Antigenic material for such a purpose can be prepared using methods known from the prior art, e.g., homogenizing the above-mentioned dermatophytes or parts thereof, fractionation of dermatophyte preparations, production of antigenic dermatophyte material by recombinant DNA technology, etc.” Altogether, the experiments provided with the Polyakov declaration are made under conditions supported by the specification of the patent application as filed.

Furthermore, the distinctions noted in the Office Action between the Example and the declaration, are only minor differences in experimental parameters that are well within the skill in the art. The MPEP states that “[w]hile care should be taken to compare the steps, material and conditions used in the experiments of the declaration with those disclosed in the application to make sure that they are commensurate in scope; i.e. that the experiments used the guidance in the specification as filed **and what was well known to one of skill in the art.**” §2164.05 (emphasis added).

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Applicants therefore respectfully submit that the declaration is evidence that must be considered.

Accordingly, Applicants submit that, based on the arguments above, the pending claims comply with 35 U.S.C. § 112, first paragraph, as well as with all other statutory requirements of the U.S. Patent Law. An applicant who complies with the statutory requirements is entitled to a patent. *In re Rouffet*, 47 U.S.P.Q.2d 1453 (Fed. Cir. 1998); *In re Oetiker*, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992); *In re Grabiak*, 226 U.S.P.Q. 870, 873 (Fed. Cir. 1985); *In re Rinehart*, 189 U.S.P.Q. 143, 147 (C.C.P.A. 1976).

Consequently, Applicants respectfully request the Examiner withdrawn the rejection.

#### **Obvious-Type Double Patenting Rejection**

Regarding the obvious-type double-patenting rejection, applicants will submit a terminal disclaimer to ensure that any patent issuing on the subject application will have the same term as the '399 patent.

In view of the foregoing it is respectfully submitted that the subject application is in condition for allowance and such favorable action at an early date is earnestly solicited.

Respectfully submitted,

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EXHIBIT A

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18

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## MEDICAL

## DICTIONARY

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**V** 1. *Vibrio*; vision; visual acuity. 2. Symbol for the element vanadium.

**V** 1. Symbol for gas flow. 2. Symbol for ventilation.

**v** L. *vena*, vein; volt.

**vaccina** (vāk-sī'nā) Vaccinia.

**vaccinable** (vāk-sin'ā-b'l) Capable of being successfully vaccinated.

**vaccinal** (vāk'sin-āl) Rel. to vaccine or to vaccination.

**vaccinate** (vāk'sin-āt) [L. *vaccinus*, pert. to cows] To inoculate with vaccine to produce immunity against disease.

**vaccination** (vāk'sī-nā'shūn) [L. *vaccinus*, pert. to cows] 1. Inoculation with any vaccine or toxoid to establish resistance to a specific infectious disease. SEE: immunization. 2. A scar left on the skin by inoculation of a vaccine.

**vaccine** (vāk'sēn, vāk-sēn') [L. *vaccinus*, pert. to cows] A suspension of infectious agents, or some part of them, given for the purpose of establishing resistance to an infectious disease. SEE: table.

Vaccines comprise four general classes:

1. Those containing living attenuated infectious organisms, such as vaccine for poliomyelitis.
2. Those containing infectious agents killed by physical or chemical means, such as vaccines used to protect human beings against typhoid fever, rabies, and whooping cough.
3. Those containing soluble toxins of microorganisms, sometimes used as such, but generally forming toxoids, such as the one used in the prevention of diphtheria and tetanus.
4. Those containing substances extracted from infectious agents, such as capsular polysaccharides extracted from pneumococci.

**FUNCTION:** Vaccines are used to stimulate an immune response in the body by creating antibodies or activated T lymphocytes capable of controlling the organism. The result is protection against a disease; the duration depends on the particular vaccine. Recovery from measles or diphtheria, for example, usually provides lifelong immunity. The immune system has produced antibodies and memory cells for these pathogens so that subsequent exposure does not result in disease. A successful vaccine does the same thing, usually without risk of illness. The measles vaccine is believed to provide lifelong immunity, but the diphtheria vaccine requires periodic booster doses. More than one type of vaccine may be available for immunization against a specific infectious agent. SEE: diphtheria;

immune response; immunity; immunization; immunobiologics.

**autogenous v.** Bacterial vaccine prepared from lesions of the individual inoculated. SYN: homologous v.

**bacterial v.** A suspension of killed, attenuated bacteria; used for injection of the body to induce development of immunity to the same organism.

**BCG v.** Bacille Calmette-Guérin preparation of a dried, living culture of *Mycobacterium tuberculosis*. In use with a high incidence of tuberculosis used in prophylactic vaccination of infants against tuberculosis. It is also in adults who are at high and unavoidable risk of becoming infected with tuberculosis. A disadvantage of use of this vaccine is that it produces hypersensitivity to tuberculin. As a result, the skin test for tuberculin sensitivity becomes positive and may persist for 5 years. There is no way to distinguish a positive skin test due to BCG from one caused by infection with *Mycobacterium tuberculosis*.

**cholera v.** A vaccine prepared from killed *Vibrio cholerae*. It is effective only a few months.

**diphtheria v.** SEE: DPT v.

**DPT v.** A combination of diphtheria, tetanus toxoids and killed pertussis cells that is administered intramuscularly to immunize children against diphtheria, tetanus, and pertussis.

**DTaP v.** A preparation of diphtheria and tetanus toxoids and acellular pertussis proteins. It may be used for the first and fifth injections in the series.

**Haemophilus influenzae type b vaccine** prepared from the bacterial capsular saccharide (HbPV) or polysaccharide conjugated to protein (HbCV).

**hepatitis B v.** A vaccine prepared from hepatitis B protein antigen produced by genetically engineered yeast.

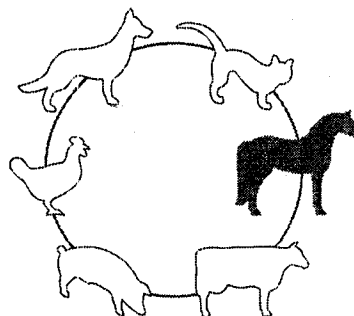
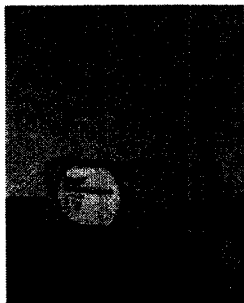
**heterologous v.** A vaccine derived from an organism different from the organism against which the vaccine is used.

**homologous v.** Autogenous v.

**human diploid cell rabies v.** An HDCV. An inactivated virus vaccine prepared from fixed rabies virus grown in human diploid cell tissue culture.

**inactivated poliovirus v.** An injectable vaccine made from three types of inactivated polioviruses. Previously used as poliomyelitis vaccine. SYN: Salk v.

**influenza virus v.** A polyvalent vaccine containing inactivated antigenic variants of the influenza virus (types A and B) either individually or combined for use in areas expected to have epidemics. Its



# Insol<sup>®</sup> Dermatophyton

*Inactivated dermatophytosis vaccine*

**D**ermatophytosis is the contagious superficial infection of the skin caused by dermatophytes (ringworm or tinea) and it is the most common skin disease in horses. The spores can survive for years. Insol(r) Dermatophyton contains highly immunogenic strains of fungus. Based on a special manufacturing process the inactivated microconidia stimulate cell-mediated immune response in particular.

Insol(r) Dermatophyton contains no adjuvants, adsorbents, additives or excipients.

## Indications

Active immunisation of horses, dogs, cats, rabbits and guinea pigs against dermatophytosis caused by trichophyton verrucosum, trichophyton mentagrophytes, trichophyton sarkisovii, trichophyton equinum, microsporum canis, microsporum gypseum and for the treatment of animals infected by dermatophytosis caused by these fungal species.

## Features

- First vaccine against dermatophytosis in horses
- Covers all relevant strains
- For prophylaxis and therapy
- Easy application/handling

## Benefits

- Comfortable way to combat dermatophytosis
- Safe for humans, safe for animals
- Vaccination during incubation possible
- 12 months protection appropriate for long term disease control

## Presentation and mode of administration

Available in 5 x 2 ml glass vials for injection  
For both prophylactic and therapeutic use 2 intramuscular injections 14 days apart on alternate sides of the body:

- horse <400 kg b.w.: 0.3 ml;  
400 - 600 kg b.w.: 0.5 ml; >600 kg b.w.: 0.7 ml
  - dogs <10 kg b.w.: 0.3 ml; 10 - 40 kg b.w.: 0.5 ml;  
>40 kg b.w.: 1.0 ml
  - cats <1 kg b.w.: 0.5 ml; >1 kg b.w.: 1.0 ml
  - rabbits <3 kg b.w.: 0.5 ml; >3 kg b.w.: 1.0 ml
  - guinea pigs: per 100 g b.w.: 0.1 ml
- repeat vaccination at yearly intervals.

Suspension  
100 Teile  
Zusammenfassung der Produkteigenschaften

## Insol® Dermatophyton Zusammenfassung der Produkteigenschaften

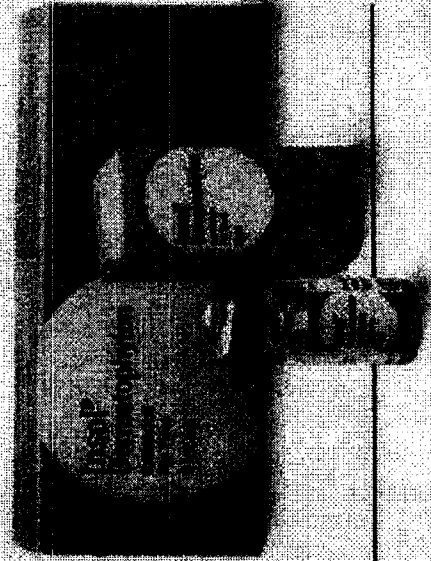
- Bei jeder Injektion sollte die Körper-  
stelle gewechselt werden.  
Zur Aufrechterhaltung des Im-  
munitäts sollten Wiederholungs-  
behandlungen nach prophylaktischer  
bzw. therapeutischer Anwendung in  
Form von zwei Injektionen im Abstand  
von 14 Tagen alle 10 bis 12 Monate  
erfolgen.
- 5.8 Überdosierung**  
Eine Überdosierung kann zu einer  
Verstärkung der aufgeführten Neben-  
wirkungen führen.
- 5.9 Besondere Warnhinweise für die  
Zubereitungen**  
keine
- 5.10 Wechselzeit**  
Es kann Gewebe vom Typ: 3 Tage
- 5.11 Besondere Vorkehrungsmaßnahmen für  
Personen bei der Anwendung des  
Produktes**  
keine
- Im Falle eines versehentlichen Ver-  
schützens des Implantates auf die Haut  
ist diese mit Wasser abzuwaschen.  
Verschüttete Selbstinjektion kann zu  
vorübergehenden Schwellungen an  
der Injektionsstelle führen. In Fällen  
schwerer Nebenwirkungen nach  
versandter Selbstinjektion mit  
dem Implantat sollte ein Arzt auf-  
gesucht werden.

### 5. Pharmazeutisches Datum

- 6.1 Unverträglichkeiten**  
Bezüglich äußerlicher Inkompatibi-  
litäten wurden keine Studien durchge-  
führt.  
Der Implantat darf nicht mit anderen  
Implantaten gemischt werden.

- 6.2 Haltbarkeit**  
Im ungeöffneten Behälter:  
36 Monate bei einer Lagerung  
zwischen +2°C bis +8°C

Boehringer Ingelheim Veterinäre GmbH  
55216 Ingelheim am Rhein  
Telefon: 0 6203 7 650 650



- Im geöffneten Behälter:  
14 Tage bei einer Lagerung  
zwischen +2°C bis +8°C.  
Sobald die Entnahme ordnungs-  
gemäß erfolgt.
- 6.3 Hinweise zur Aufbewahrung**  
Der Implantat ist zwischen +2°C und  
+8°C zu lagern!  
Nicht einfristen! Vor Licht schützen!  
Implantat für Kinder unzugänglich  
aufbewahren!
- 6.4 Behälter**  
2 ml-, 5 ml-, oder 10 ml-Glasflaschen  
des Glaxo L verschlossen mit Brom-  
butyl-Gummistopfen und Aluminium-  
brüchekappen
- 6.5 Zulassungsinhaber**  
Boehringer Ingelheim  
Vetmedica GmbH  
55216 Ingelheim  
Hergestellt  
Serumwerk Marzen  
23118 Hoyerberg
- 6.6 Besondere Hinweise für die Bezuhr-  
gung von unbrauchbarem Material**  
Leere Behälter, nicht völlig aufge-  
braucht oder nach Ablauf des  
Verfallsdatums nicht mehr verwend-  
barer Implantat sind unschädlich zu  
besorgen.

### 7. Weitere Informationen

Zulassungs-Nummer: 118a/96  
Datum der Genehmigung dieser Zusam-  
menfassung der Produkteigenschaften:  
24.01.2000  
Abgabeweise: Verschreibungsabhängig  
Zugelassene Handelsform:  
Packung mit 2 ml  
Packung mit 5 x 2 ml

# **Insol® Dermatophyton** Zusammenfassung der Produkteigenschaften

<b>1. Name</b>	
<b>Insol® Dermatophyton</b>	
<b>1. Zusammensetzung</b>	
1 ml der inaktivierten Vakzine enthält jeweils mind. 6,25 x 10 <sup>5</sup> Mikrokonidien der folgenden Pilzstämme:	
- <i>Trichophyton verrucosum</i> , Stamm Nr. 410	
- <i>Trichophyton mentagrophytes</i> , Stamm Nr. 1032	
- <i>Trichophyton sarkisovi</i> , Stamm Nr. 551	
- <i>Trichophyton equinum</i> , Stamm Nr. 381	
- <i>Mikrosporum canis</i> , Stamm Nr. 1393	
- <i>Mikrosporum canis</i> var. <i>distortum</i> , Stamm Nr. 120	
- <i>Mikrosporum canis</i> var. <i>obesum</i> , Stamm Nr. 1311	
- <i>Mikrosporum gypseum</i> , Stamm Nr. 59	

und maximal 0,044 mg Thiomersal in einer Glucose-Flüssigkeits-Suspension

<b>3. Darreichungsform</b>	
Suspension zur Injektion	
<b>4. Immunologische Eigenschaften</b>	
Die Verabreichung des Impfstoffes bewirkt die Ausbildung einer Immunität bei Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophyosen, verursacht durch <i>Trichophyton verrucosum</i> , <i>Trichophyton mentagrophytes</i> , <i>Trichophyton sarkisovi</i> , <i>Trichophyton equinum</i> , <i>Mikrosporum canis</i> und <i>Mikrosporum gypseum</i> .	
Die im Impfstoff enthaltenen Stämme sind tierischen Ursprungs. <i>Trichophyton verrucosum</i> (Stamm Nr. 410) wurde von einem Renntier, <i>Trichophyton mentagrophytes</i> (Stamm Nr. 1032) von einem Pferd, <i>Trichophyton sarkisovi</i> (Stamm Nr. 551) von einem Kameel, <i>Trichophyton equinum</i> (Stamm Nr. 381) von einem Pferd,	

*Mikrosporum canis* (Stamm Nr. 1393) von einer Katze, *Mikrosporum canis* var. *distortum* (Stamm Nr. 120) von einem Schwein, *Panther*, *Mikrosporum canis* var. *obesum* (Stamm Nr. 1311) von einem Tiger und *Mikrosporum gypseum* (Stamm Nr. 59) von einem Pferd isoliert.

Die erzeugte Immunität ist hauptsächlich ohne Zell-vermittelte Immunantwort und hält in der Regel 10 bis 12 Monate an.

<b>5. Klinische Daten</b>	
<b>5.0 Zielherarten</b>	
Pferde, Hunde, Katzen, Kaninchen und Meerschweinchen	
<b>5.1 Anwendungsgebiete</b>	
Zur aktiven Immunisierung von Pferden, Hunden, Katzen, Kaninchen und Meerschweinchen gegen Dermatophyosen, verursacht durch <i>Trichophyton verrucosum</i> , <i>Trichophyton mentagrophytes</i> , <i>Trichophyton sarkisovi</i> , <i>Trichophyton equinum</i> , <i>Mikrosporum canis</i> und <i>Mikrosporum gypseum</i> zum Zwecke der Reduktion des Risikos einer klinischen Infektion durch diese Pilzarten, sowie als tierärztliche Maßnahme zur Beschleunigung der Abheilung der klinisch sichtbaren Hautveränderungen bei Tieren, die an einer durch diese Pilzarten verursachten Dermatophyose erkrankt sind.	

<b>5.2 Gegenanzeigen</b>	
Tiere mit Fieber und/oder mit dermatophyosenähnlichen Symptomen einer Infektions-Erkrankung, sowie Tiere, die unter Kortikoid-Wirkung stehen, sollten nicht geimpft werden. Jungtiere entsprechend den folgenden Angaben sind von einer Impfung auszuschließen:	
Pferde unter 5 Monaten	
Hunde unter 6 Wochen	
Katzen unter 1 Monat	
Kaninchen unter 6 Wochen	
Meerschweinchen unter 150 g	
Nicht geimpft werden dürfen gestresste Tiere, z.B. Pferde im Auktionsstress	

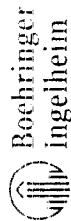
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<b>5.3 Nebenwirkungen</b>	
Nach der Injektion können, besonders bei Pferden, bis zu höherergrade Schwellungen an der Injektionsstelle auftreten, die innerhalb von 3 bis 5 Tagen ohne weitere therapeutische Maßnahmen abheilen. In Einzelfällen wurden schmerzhaft, bis zu handflächengroße Schwellungen an der Injektionsstelle in Verbindung mit gestörtem Allgemeinbefinden (z.B. Fieber, Inappetenz, Apathie) beobachtet, die innerhalb von 2 bis 10 Tagen abgeklungen waren. In solchen Fällen ist eine symptomatische Behandlung zu empfehlen, wobei von lokal setzenden Mitteln abgesehen werden sollte.	
<b>5.4 Besondere Hinweise für den Gebrauch</b>	
Bei Tieren, die sich zum Zeitpunkt der Impfung im Inkubationsstadium befinden, kann es trotz Impfung zum Ausbruch der Erkrankung kommen. Die Hautveränderungen heilen jedoch innerhalb von 2 bis 4 Wochen nach 2. Injektion ab.	
Da sich auch im Haarfeld der Tiere Dermatophyose-Erreger befinden können und diese durch die Impfung nicht erreicht werden, ist das Zoonosen-Risiko durch die Impfung zwar deutlich verringert, aber nicht vollständig auszuschließen. Aus diesem Grunde, sowie auch zur Senkung des Infektionsrisikos, ist bei langhaarigen Tieren das Scheren der Haare zu empfehlen. Aus dem gleichen Grunde wird empfohlen, auch solche Tiere zu impfen, die in direktem oder indirektem Kontakt zu infizierten Tieren stehen. Zur Reduktion des allgemeinen Infektionsrisikos sollten außerdem Reinigungs- und Desinfektionsmaßnahmen der Umgebung sowie des Gebrauchsgegenstands (z.B. Putzzeug) durchgeführt werden.	
Erfahrungen aus der Praxis haben gezeigt, dass insbesondere in Edelekatzenbesitz, in denen ein erhöhter Infektionsdruck zu erwarten ist, eine verminderte Wirksamkeit auf-	

<b>5.5 Anwendung während Trächtigkeit und Laktation</b>	
Aufgrund des Manipulationsstresses sollen Impfungen zu Beginn und gegen Ende der Trächtigkeit allgemein ein Risiko dar und sollten deshalb vermieden werden.	
<b>5.6 Wechselwirkungen</b>	
Studien zu möglichen Wechselwirkungen wurden nicht durchgeführt. Es wird jedoch empfohlen, zwischen den Impfungen, sowie innerhalb von 14 Tagen vor und nach den Impfungen keine anderen Immunisierungen vorzunehmen.	
<b>5.7 Dosierung und Art der Anwendung</b>	
Vor Gebrauch gut schütteln! Die Impfdosis beträgt für:	
<b>Pferde:</b>	
unter 400 kg KGW 0,3 ml	
400 - 600 kg KGW 0,5 ml	
über 600 kg KGW 0,7 ml	
<b>Hunde:</b>	
bis 10 kg KGW 0,3 ml	
10 bis 40 kg KGW 0,5 ml	
über 40 kg KGW 1,0 ml	
<b>Katzen:</b>	
bis 1,0 kg KGW 0,5 ml	
über 1,0 kg KGW 1,0 ml	
<b>Kaninchen:</b>	
bis 3,0 kg KGW 0,5 ml	
über 3,0 kg KGW 1,0 ml	
<b>Meerschweinchen:</b>	
pro 100 g KGW 0,1 ml	
Sowohl zur Prophylaxe als auch zur Therapie sind 2 intramuskuläre Injektionen im Abstand von 14 Tagen erforderlich.	
Ist bei an einer Dermatophyose erkrankten Tieren zwei Wochen nach zweiter Injektion noch keine eindeutige Verbesserung der Haut- und Haardefekte erkennbar, wird eine dritte Injektion empfohlen.	
Auf eine strenge intramuskuläre Injektion ist zu achten; eine subkutane Injektion ist unbedingt zu vermeiden.	

ten kann bzw. eine Rezidivneigung beobachtet werden kann.

# Insol® Trichophyton



Inactivated trichophytosis vaccine for cattle

## Aqueous suspension for intramuscular injection

### Composition

1 ml of inactivated vaccine contains:  
at least  $17 \times 10^6$  microconidia of each  
of the following strains of fungi:

- Trichophyton verrucosum, strain no. 410
- Trichophyton mentagrophytes, strain no. 1032
- Trichophyton sarkisovii, strain no. 551

and a maximum of 0.040 mg thimerosal

in a glucose meat extract suspension

### Indications

Active immunisation of cattle from the age of 1 month onwards against trichophytosis caused by Trichophyton verrucosum, Trichophyton mentagrophytes and/or Trichophyton sarkisovii and as an aid in the treatment of cattle infected by trichophytosis caused by these fungal species.

### Contraindications

None.

### Undesirable effects

Slight swelling can occur at the injection site (mostly after accidental subcutaneous injection) which clears with no adverse symptoms.

In exceptional cases (ca. 0.05%) shock reactions in the form of dyspnoea, pulmonary oedema, reddish foam around the mouth and nose and heavy transpiration can occur (death can

occur in ca. 0.01% of the vaccinated animals). In such cases symptomatic treatment including administration of adrenalin, glucocorticoids and antihistamines, possibly together with a dose of calcium, is indicated.

### Special Precautions for use

In the case of animals which are in the incubation phase at the time of vaccination, the disease can still break out in spite of the vaccination. However, the skin lesions heal 2-4 weeks after the second injection.

### Use during pregnancy and lactation

The vaccination can be carried out at any stage of pregnancy. To date no effect on milk output has been observed.

### Interactions

No interaction studies have been performed.

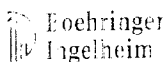
However, it is recommended that no other immunisations be carried out between the vaccinations or within 14 days before and after the vaccinations.

### Posology and method of administration

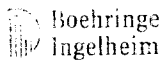
Shake well before use.

The vaccination dose is for cattle with less than 70 kg bodyweight: 2.5 ml  
for cattle with more than 70 kg bodyweight: 5.0 ml

aqueous suspension for intramuscular injection.  
Carefully follow the instructions for use.  
The inactivated vaccine contains at least  $17 \times 10^6$  microconidia of each of the following strains of fungi:  
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and a maximum of 0.040 mg thimerosal in a glucose meat extract suspension.



Withdrawal Periods:  
Edible Tissue: 3 days  
Milk: none

**Storage:**  
Store at between +2°C and +8°C.  
Do not freeze. Protect from light.  
Once the bottle has been opened, the vaccine may be used for up to 14 days if extracted properly and stored in a cool place.

**FOR ANIMAL TREATMENT ONLY  
KEEP OUT OF REACH OF CHILDREN**

Authorisation No: AR8/003/01

Boehringer Ingelheim Limited,  
Ellesfield Avenue, Bracknell  
Berks., RG12 8YS

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9038  
V 10153/IE/1

9038  
V 10153/IE/1

Expiry Date:

Expiry Date:

Batch No.:

Batch No.:

EXHIBIT C

Both for prophylaxis and for therapy 2 intramuscular injections with a 14-day interval are required. The injections should be given on alternate sides of the body. To maintain the vaccine protection after prophylactic or therapeutic administration, repeat vaccinations should be carried out at yearly intervals.

Subcutaneous injection is to be avoided

**Overdose**

Can lead to slight local intolerance reactions.

**Special warnings for the target species**

Animals with fever and/or symptoms of an infectious disease other than trichophytosis and animals which are still under the influence of corticosteroids should not be vaccinated. Animals under 4 weeks of age should not be vaccinated. Do not vaccinate stressed animals, for example animals for which a new strawbedding has been freshly prepared.

**Withdrawal periods**

Edible tissue: 3 days  
Milk: none

**Special precautions to be taken by the person administering the product to animals**

None.

Rinse with water if the vaccine is accidentally spilled onto the skin. Accidental self injection may lead to mild transient swelling at the injection site. In case of severe side effects following an accidental self injection of vaccine a medical surgeon should be consulted.

**Incompatibilities**

No incompatibility studies have been performed.

**Storage**

Store at between +2°C and +8°C. Do not freeze. Protect from light.

If stored at between +2°C and +8°C and as long as the vaccine is removed from the vial correctly, the vaccine may be used for up to 14 days after the vial has been opened.

**Pack sizes**

50 ml, 100 ml or 250 ml glass vials.

**Warnings**

For animal treatment only.

Keep vaccine out of the reach of children.

Do not use vaccine after the expiry date.

Empty containers and vaccine which is no longer usable after the expiry date are to be disposed of safely according to national requirements.

**Manufacturer**

Serumwerke Memsen  
D-27318 Hoyerhagen  
Germany

Authorisation No. AR8/003/01

**Boehringer Ingelheim Limited**  
Ellesfield Avenue  
Bracknell, Berkshire  
RG12 8YS

This leaflet was written  
in March 1998.

**Insol®**  
**Trichophyton**  
Inactivated trichophytosis  
vaccine for cattle  
100 ml

LM

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**Boehringer**  
**Ingelheim**

Boehringer Ingelheim Limited  
Ellesfield Avenue, Bracknell  
Berks., RG12 8YS

LM

# Insol<sup>®</sup> Trichophyton

Inactivated trichophytosis  
vaccine for cattle

100 ml



Boehringer  
Ingelheim



5 012917 021004

Batch No.:

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V 10155/IE/1